REMARKS

After entry of this amendment, claims 1, 3-20, and 22-34 are pending. Claims 1, 3, 20, and 22 are amended to expedite prosecution. New claims 33 and 34 are supported by original claims 3 and 22.

Double Patenting Rejection

Further reconsideration is respectfully requested of the rejection of claims 1-34 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,265,386 (the '386 patent). The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.[1] However, an important distinction applies. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.[2]

The subject matter of the claims of the instant application would not have been obvious in view of claims 1-25 of the '386 patent. When evaluating the scope of a claim, every element of the claim must be considered.[3] To support an obviousness-type double patenting rejection, there must be some motivation or suggestion in the art to modify the methods of the '386 patent to incorporate the features of the instantly claimed methods. It is respectfully submitted that the Office has failed to establish any such motivation or suggestion, either by citation of a secondary reference or by evidence of the level of skill in the art or the nature of the problem.

---

[1] In re Braat, 937 F.2d 589 (Fed. Cir. 1991).

[2] Purdue Pharma L.P. v. Boehringer Ingelheim GMbH, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

[3] See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).

Subject claim 1 is directed to a method for preventing or reducing mucositis in a patient exposed to radiation, the method comprising administering to said patient an effective amount of a protective agent. In contrast, claims 1-25 of the '386 patent are generally directed to methods for preventing or treating ototoxicity in a patient undergoing treatment with an aminoglycoside antibiotic by administering an otoprotective agent comprising D-methionine. Accordingly, as the claims of the '386 patent do not include the elements of "preventing or reducing mucositis" or a "patient exposed to radiation," the claims do not include all the elements of the subject claims. Furthermore, the claims of the '386 patent would not have motivated a person of ordinary skill to administer methionine to a patient suffering mucositis; and certainly would have failed to create any expectation that mucositis would or could be alleviated by administration of methionine. The '386 claims offer no remote suggestion that administration of methionine could be expected to prevent or alleviate mucositis induced by radiation. The claims of the '386 patent deal neither with radiation nor with mucositis. Instead, they deal solely with treatment of ototoxicity from administration of an aminoglycoside antibiotic.

35 U.S.C. § 102 Rejection

Reconsideration is respectfully requested of the rejection of claims 1-34 as being anticipated by U.S. Patent No. 6,265,386 (Campbell). A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation.[4] Because the Campbell patent does not mention nor provide the remotest suggestion that methionine or methionine-like moieties would have any value in dealing with mucositis resulting from radiation exposure or administration of anti-tumor platinum-coordination compounds, the patent does not expressly anticipate the subject claims.

[4] Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc., 976 F.2d 1559, 1565 (Fed. Cir. 1992).

Claims 1, 3-19, and 33

Further, the Campbell patent does not inherently anticipate subject claims 1, 3-19, and 33. In general, inherent anticipation may not be established if there is only a possibility or even a probability that a certain result may occur.[5] The subject matter of the claim must inevitably be achieved in the replication of the reference's teachings for inherency to be found.[6] In this case, radiation exposure as described in the Campbell patent does not inevitably result in mucositis. For example, radiation treatment is usually targeted to a specific area of the body wherein the diseased tissue is located. Thus, different side effects arise depending on the location of the diseased tissue. For example, mucositis may develop in patients receiving radiation treatment wherein mucosal tissue is in the field of the radiation exposure. In particular, oral mucositis commonly develops in treatment of cancers in the oral cavity or nasopharyngeal area due to the proximity of the oral mucosa to the tissues targeted by radiation treatment. In contrast, when the diseased tissue targeted for radiation treatment is not in proximity to mucosal tissue, mucositis will not inevitably arise from the radiation treatment. By way of example, radiation treatment of a breast tumor or tissue proximate to a surgically removed breast tumor does not necessarily result in mucositis because mucosal tissue is not in close proximity to the diseased breast tissue. Of course, radiation may cause problems other than mucositis in the tissue targeted. In fact it usually does; but these effects have no relevance to the method herein claimed. Examples of side effects arising from damage to healthy tissue, other than mucosal tissue, that is in the field of radiation exposure are appetite loss from radiation damage to brain cells, gastrointestinal disorders from radiation damage to cells in the gastrointestinal tract and/or abdomen, and neurotoxicity from damage to nerve cells.

---

[5] In re Oelrich, 666 F.2d 578.

[6] Continental Can Co. v. Monsanto Co., 948 F.2d, 1264, 20 U.S.P.Q.2d 1746 (Fed. Cir. 1991).

Claims 20, 22-32, and 34

Additionally, the Campbell patent does not anticipate claims 20, 22-32, and 34. Mucositis resulting from treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound occurs in fewer patients than other side effects such as, for example, ototoxicity, neurotoxicity, weight loss, and alopecia. Specifically, the cisplatin dosages exemplified in the Campbell patent would not inevitably have resulted in mucositis. Thus, a patient receiving treatment with an anti-tumor platinum-coordination compound could develop ototoxicity, neurotoxicity, weight loss, and alopecia, and not inevitably develop mucositis.

In summary, because the Campbell patent does not expressly or inherently disclose all the limitations of claims 1, 3-20, and 22-34, these claims are patentable over the Campbell patent.

35 U.S.C. § 103 Rejection

Reconsideration is respectfully requested of the rejection of claims 1-32 as unpatentable over U.S. Patent No. 6,265,386 (Campbell) in view of U.S. Patent No. 4,961,926 (Gabrilove). It is respectfully noted that the Campbell patent makes no mention of mucositis resulting from any type of insult; and that the patent contains not the remotest suggestion that methionine or methionine-like moieties would have any value in dealing with mucositis resulting from radiation exposure or administration of an anti-tumor platinum-coordination compound. Although the Campbell patent discloses methionine as a protectant for gastrointestinal disorders, not all of these gastrointestinal disorders are mucositis-related disorders. Further, gastrointestinal toxicity as described in the Campbell patent includes nausea, vomiting, esophageal reflux, stomatitis, bleeding in the gastrointestinal tract, diarrhea, weight loss, and/or anorexia.[7] Some of these toxicities can be caused by damage to cells located in areas other than the gastrointestinal tract. For example, a cause of nausea and vomiting is radiation treatment of a brain tumor; the treatment causes damage to healthy cells surrounding

[7] U.S. Patent No. 6,265,386, column 13, lines 11-19.

the tumor and that damage can result in nausea and vomiting. Thus, from this disclosure alone, it would not have been obvious to a person of skill in the art that methionine would be a protectant for mucositis.

Gabrilove discloses methods of preventing mucositis comprising administering granulocyte colony stimulating factor (GCSF) or a polypeptide analog thereof. In particular, the GCSF analog may be a nonglycosylated polypeptide having an amino acid sequence identical to the sequence of the polypeptide component of naturally occurring GCSF except for the presence of an additional methionine at the N-terminus.

The combination of the Campbell and Gabrilove patent disclosures does not render the instant claims unpatentable. For such a combination to be proper, there must be some motivation in the prior art or knowledge in the art to combine the teachings. In this case, Gabrilove discloses administration of proteins and polypeptides as therapeutic agents to prevent mucositis, but the Campbell patent does not contemplate proteins or polypeptides as protective agents. Thus, a person of skill in the art would not have been motivated to substitute methionine from the Campbell patent for the protein or polypeptide of the Gabrilove patent to arrive at the instant claims.

Accordingly, it is respectfully submitted the record fails to include evidence on which to base a rejection of the claims for obviousness, and that the current rejection under §103 be withdrawn.

SIU 7397
PATENT

CONCLUSION

Applicant submits that the present application is now in a condition for allowance and requests early allowance of the pending claims.

The Commissioner is authorized to charge Deposit Account 19-1345 in the amount of $100.00 for one additional independent claim. The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,

John K. Roedel, Jr., Reg. No. 25,914
SENNIGER POWERS
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

JKR/JSH/dep

MAIL STOP AMENDMENT
VIA FACSIMILE NO. 571-273-8300